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A Study of Some New Hydroxamic Acids of Hydroxy and Alkoxy Fatty Acids

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A Study of Some New Hydroxamic Acids of Hydroxy and Alkoxy Fatty Acids

A DISSERTATION

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BY

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A STUDY OF SOME NEW HYDROXAMIC ACIDS OF HYDROXY AND ALKOXY FATTY ACIDS

Introduction

The rearrangement of hydroxamic acids (Lossen), of acid azides (Curtius), of halogen amides (Hofmann), and other related classes of compounds is believed to occur in two steps.[1]

$$R{-}C(=O)N\begin{matrix}\nearrow x \\ \searrow y\end{matrix} \longrightarrow R{-}C(=O)N\begin{matrix}\nearrow \\ \searrow\end{matrix} + xy \qquad (1)$$

$$R{-}C(=O)N\begin{matrix}\nearrow \\ \searrow\end{matrix} \longrightarrow RN{=}C{=}O$$

The final rearrangement products depend upon experimental conditions. Thus, when an alkali salt of an acyl ester of a monohydroxamic acid, RCON(K)OCOR′, is heated alone, the isocyanate may be isolated; but when it is heated with water, the isocyanate generally reacts to give an amine or a disubstituted urea, and when alcohol is employed as a solvent, a urethan is usually formed.

Without considering the mechanism of these reactions in detail, it may be pointed out that Stieglitz and his associates have made extensive investigations to determine the influence which variations of the groups, x and y, have on the ease of rearrangement of such compounds.[2] But little attention has been paid to the effects produced by varying the radical R. Jones and Hurd,[3] who studied monophenyl-, diphenyl-, and triphenylacethydroxamic acids, found that the triphenylmethyl radical rearranged with great readiness. They concluded that the ease of rearrangement of the radical R was dependent in some way upon the ability of this group R to exist as a free radical. This was extended by Hurd to derivatives of N-phenyl-hydroxy-urethan and of N-diphenyl-hydroxy-urethan, $(C_6H_5)_2$-NCON(K)OCOCH$_3$; since the radical $(C_6H_5)_2N$ may exist as a free radical, this compound rearranged to give unsymmetrical diphenylhydrazine, but

[1] Stieglitz, *Am. Chem. J.*, **18**, 751 (1896); **29**, 51 (1903). Jones, *Am. Chem. J.*, **50**, 440 (1913).

[2] Stieglitz and Slossen, *Ber.*, **34**, 1613 (1901). Stieglitz, *Am. Chem. J.*, **29**, 49 (1903). Stieglitz and Higbee, *ibid.*, **29**, 52 (1903). Stieglitz and Earle, *ibid.*, **30**, 399 (1904). Stieglitz, *J. Am. Chem. Soc.*, **36**, 288 (1914). See also, Jones, *Am. Chem. J.*, **48**, 1 (1912); **50**, 414 (1913); *J. Am. Chem. Soc.*, **36**, 1268 (1914).

[3] Jones and Hurd, *J. Am. Chem. Soc.*, **43**, 2422 (1921).

no rearrangement of the radical C_6H_5NH was observed in the case of the monophenyl-hydroxy-urethan.

We have continued the investigation in order to determine the effects produced when oxygen forms a part of the rearranging group R. For this purpose hydroxy-, methoxy-, and ethoxy-acethydroxamic acids, and β-methoxy-propionhydroxamic acid together with their benzoyl and acetyl esters and some of their salts have been prepared. By rearrangement the alkoxy hydroxamic acids should give new ether-isocyanates, amino-ethers, and ether-ureas, which in themselves should be of interest.

Hydroxy-acethydroxamic Acid and Its Derivatives

This acid, prepared by the action of ethyl glycollate upon hydroxylamine, is a colorless solid which melts at 85°. It would be expected that the potassium salt of its benzoyl ester, dissolved in alcohols, would rearrange to give potassium benzoate and N-hydroxymethyl-urethans.

$$HOCH_2CON\begin{matrix}K\\ \diagdown\\ \diagup\\ OCOC_6H_5\end{matrix} \longrightarrow C_6H_5COOK + HOCH_2N{=}C{=}O \qquad (2)$$

$$HOCH_2N{=}C{=}O + HOR \longrightarrow CH_2(OH)NHCOOR$$

When this salt was dissolved in boiling *iso*-amyl alcohol, rearrangement occurred but no N-hydroxymethyl-urethan was produced. In its stead, formaldehyde and *iso*-amyl allophanate, $NH_2CONHCOOC_5H_{11}$, m. p., 160°, were isolated. The potassium salt was not affected by boiling ethyl alcohol, but rearranged when it was heated with it for four hours at 120°. Formaldehyde, potassium benzoate, and ethyl allophanate, m. p., 191°, were obtained as products of the reaction.

The resistance to rearrangement displayed by the salt in the presence of boiling ethyl alcohol is duplicated in its behavior towards water. When the salt was dissolved in boiling water, no rearrangement could be detected, but it was hydrolyzed to form the benzoyl ester to the extent of 95%.

$$CH_2(OH)CON(K)OCOC_6H_5 + HOH \rightleftharpoons CH_2(OH)CON(H)OCOC_6H_5 + KOH \qquad (3)$$

It is difficult to explain the formation of allophanates in terms of the mechanism usually proposed for similar reactions. However, hydroxymethyl isocyanate, $CH_2(OH)N{=}C{=}O$, which would be formed first as a product of rearrangement, may be regarded as an addition product of cyanic acid to formaldehyde, and it is well known that compounds of this type show a decided inclination to regenerate formaldehyde. If such a dissociation occurred in this instance,

$$CH_2(OH)N{=}C{=}O \longrightarrow H_2C{=}O + HN{=}C{=}O \qquad (4)$$

the final substances obtained by rearrangement would be determined by the action of alcohols upon these products.

Liebig and Wöhler[4] showed that cyanic acid reacted with alcohols at ordinary temperatures to give allophanic esters and since that time a

[4] Liebig and Wöhler, *Ann. Chem. Pharm.*, **20**, 396 (1830).

large number of such esters have been prepared in this way.[5] These

$$2HNCO + C_2H_5OH \longrightarrow NH_2CONHCO(OC_2H_5) \quad (5)$$

relations explain completely the apparent anomaly in the rearrangement of derivatives of hydroxy-acethydroxamic acid.

The similarity in rearrangement of hydroxamic acids (Lossen) and acid azides (Curtius) has been pointed out frequently. It would be interesting, therefore, to ascertain whether hydroxy-acetazide, $CH_2(OH)CON_3$, which should yield hydroxymethyl isocyanate, actually shows a corresponding departure from the normal in its reaction with alcohol.

Curtius and Heidenreich[6] who prepared hydroxy-acetazide, claim that it rearranged in ethyl alcohol to give N-hydroxymethyl-urethan (see Equation 2). Their product melted at 189°. They state that, on hydrolysis with moderately strong mineral acid, it gave ammonia, carbon dioxide, ethyl alcohol and some formaldehyde.

In 1908, however, Einhorn and Hamberger[7] prepared N-hydroxymethyl-urethan and found that it melted at 53°, and when treated with moderately strong mineral acid gave methylene-diurethan, a compound melting at 131°, previously described by Conrad and Hock.[8] Curtius and Heiden-

$$2CH_2(OH)NHCOOC_2H_5 \longrightarrow CH_2(NHCOOC_2H_5)_2 + H_2O + HCHO \quad (6)$$

reich in 1895 showed that this same methylene derivative, obtained by them as an oil from malonylazide, $CH_2(CON_3)_2$, was hydrolyzed only with difficulty to give ammonia, carbon dioxide, ethyl alcohol and formaldehyde. It was necessary to heat it in a sealed tube with dil. sulfuric acid at 150°. These facts make it highly improbable that Curtius and Heidenreich could have obtained N-hydroxymethyl-urethan by the rearrangement of hydroxy-acetazide in ethyl alcohol.

Furthermore, since the melting point of their product, 189°, is only 2° below that of ethyl allophanate, 191°, which we obtained in our reaction, it seems certain that the compound isolated by them must have been ethyl allophanate, possibly containing a small amount of formaldehyde which would be formed simultaneously.

Lactazide, $CH_3CH(OH)CON_3$, and mandelazide, $C_6H_5CH(OH)CON_3$, two other α-hydroxy azides which were prepared by Curtius and his students,[9] rearranged in alcohol to give acetaldehyde and benzaldehyde, respectively, and both azides gave *allophanic ester*. They explained the products thus,

$$RCH(OH)CON_3 + C_2H_5OH \longrightarrow N_2 + RCH(OH)NHCOOC_2H_5$$
$$2RCH(OH)NHCOOC_2H_5 \longrightarrow 2RCHO + NH_2CONHCOOC_2H_5 + C_2H_5OH \quad (7)$$

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[5] Traube, *Ber.*, **22**, 1572 (1889). Grandiere, *Bull. soc. chim.*, **35**, 187 (1924).

[6] Curtius and Heidenreich, *J. prakt. Chem.*, [2] **52**, 225 (1895).

[7] Einhorn and Hamberger, *Ann.*, **361**, 130 (1908).

[8] Conrad and Hock, *Ber.*, **36**, 2206 (1903).

[9] Curtius and Müller, *Ber.*, **34**, 2794 (1901).

and based these equations on the work of Loeb[10] who showed that urethan and phosgene, heated in a sealed tube with benzene, gave allophanic ester. But these experimental conditions are entirely different from those involved in the evaporation of an alcohol solution of the azide, and it has been shown that urethans may be used instead of cyanic acid in certain synthetic reactions.[11]

Curtius and Müller proposed the hypothesis that acid azides possessing the group CHOH would give allophanic esters, while those having a group CH_2OH would give hydroxy-urethans; but the explanation advanced to account for the rearrangement of hydroxy-acethydroxamic acid and hydroxymethyl-acetazide serves equally well for these α-hydroxy-azides. Cyanic acid, formed in each case, reacts with the alcohol to yield

$$\begin{aligned} CH_3CH(OH)CON_3 &\longrightarrow CH_3CH(OH)NCO \longrightarrow CH_3CHO + HNCO \\ C_6H_5CH(OH)CON_3 &\longrightarrow C_6H_5CH(OH)NCO \longrightarrow C_6H_5CHO + HNCO \end{aligned} \qquad (8)$$

allophanic ester.

Our experience with hydroxy-acethydroxamic acid and the experimental work presented above have led us to the following hypothesis. Any substance (bromo-amide, hydroxamic acid, acid azide, etc.) which has an hydroxyl group in the α-position, when it undergoes a rearrangement of the Hofmann-Curtius-Lossen type, will give an aldehyde or ketone and cyanic acid. If rearrangement takes place in aqueous solution, cyanic acid will yield urea or carbon dioxide and ammonia, and in alcohol an allophanic ester will be formed. The fact that hydracryl azide, $CH_2OHCH_2CON_3$, yields no allophanic ester may be attributed rather to the absence of an α-hydroxyl group than to the presence of the group CH_2OH.

Jones and Neuffer[12] found that the benzoyl esters of lacthydroxamic acid, $CH_3CH(OH)CONHOCOC_6H_5$, and of mandelhydroxamic acid, $C_6H_5CH(OH)CONHOCOC_6H_5$, when heated with water gave acetaldehyde and benzaldehyde, respectively, accompanied by benzoic acid, carbon dioxide and ammonia, in accord with the hypothesis proposed above. The formation of some *sym*-dibenzoyl urea in both cases[13] is difficult to explain; possibly cyanic acid may react with benzoic acid to give this product. Recently it has been shown[14] that symmetrical disubstituted ureas are obtained when certain aromatic hydrocarbons are heated with substances which yield cyanic acid.

Methoxy-acethydroxamic Acid and Ethoxy-acethydroxamic Acid

These hydroxamic acids were prepared by the action of hydroxylamine upon the esters or chlorides of the corresponding alkoxy-acetic acids.

[10] Loeb, *Ber.*, **19**, 2344 (1886).
[11] Bamberger, *Ber.*, **23**, 1836 (1890).
[12] Jones and Neuffer, *J. Am. Chem. Soc.*, **39**, 659 (1917).
[13] Ref. 12, p. 661.
[14] Curtius and Schmidt, *J. prakt. Chem.*, **105**, 177 (1923).

The former melts at 85.5° and the latter at 74–76°. They are the first representatives of ether or alkoxy hydroxamic acids of the aliphatic series. In order to study the rearrangement of these compounds, their benzoyl and acetyl esters and some of the salts of these esters were prepared.

If the reaction proceeded in the usual fashion, the salts of these acyl esters should rearrange in the presence of water as follows.

$$\left.\begin{aligned} ROCH_2C(=O)N(K)OCOC_6H_5 &\longrightarrow C_6H_5COOK + ROCH_2N=C=O \\ ROCH_2N=C=O + H_2O &\longrightarrow ROCH_2NH_2 + CO_2 \\ ROCH_2N=C=O + ROCH_2NH_2 &\longrightarrow (ROCH_2NH)_2CO \end{aligned}\right\} (9)$$

But a study of the isocyanates showed that the reactions did not follow this course.

When the dry potassium salts of the benzoyl esters were heated, a sudden puff occurred between 115° and 120°, the products of rearrangement were potassium benzoate, and the isocyanates, $ROCH_2NCO$, which were distilled and isolated. These ether-isocyanates, also, represent the first members of a new class of aliphatic compounds. We have prepared them by the action of silver cyanate on chloromethyl-methyl ether and chloromethyl-ethyl ether.

Experiments showed that the amines, $ROCH_2NH_2$, produced by hydrolysis of these isocyanates are unstable and dissociate at once to give alcohols, ammonia and formaldehyde. Consequently, the hydrolysis of the isocyanate proceeds as follows.

$$\left.\begin{aligned} ROCH_2N=C=O + H_2O &\longrightarrow ROCH_2NH_2 + CO_2 \\ ROCH_2—NH_2 &\longrightarrow ROH + CH_2=NH \\ CH_2=NH + H_2O &\longrightarrow HCHO + NH_3 \end{aligned}\right\} (10)$$

A small amount of hexamethylene-tetramine was isolated, but no symmetrically disubstituted ureas could be found.

Experiments were made to isolate methoxy- and ethoxy-methylamine. N-methoxy-methyl phthalimide, $C_6H_4(CO_2)_2NCH_2OCH_3$, was hydrolyzed under conditions as favorable as possible, but it gave the decomposition products of the amine (Equation 10). Chloromethyl-methyl ether was passed into cold ether saturated with ammonia. A white solid was precipitated which consisted of ammonium chloride, formaldehyde, and hexamethylene-tetramine. There was no evidence of the formation of a chloride, $CH_3OCH_2NH_3Cl$.[15]

β-Methoxy-propionhydroxamic Acid and Its Derivatives

This acid, m. p., 93–95°, was prepared by the action of hydroxylamine upon methyl β-methoxypropionate, or upon β-methoxypropionyl chloride. The second method was found to be the more satisfactory. The benzoyl and acetyl esters and their salts were made.

[15] In 1885 Hofmann found that the bromo-amide of ethoxy-acetic acid [Hofmann, *Ber.*, **18**, 2736 (1885)] rearranges in the presence of alkali to give α-ethoxymethyl-β-ethoxyacetyl urea, $C_2H_5OCH_2NH—CO—NHCOCH_2OC_2H_5$. Hydrolysis of this urea did not give ethoxymethylamine but the decomposition products of this amine.

It was expected that the salts of the benzoyl ester of this acid would rearrange to give *sym*-dimethoxyethyl urea. (See Equation 9.) This urea should be stable in aqueous solution, since ethoxyethylamine, $C_2H_5OCH_2CH_2NH_2$, which was isolated by Knorr,[16] is not easily decomposed by water. When the potassium salt was dissolved in boiling water, rearrangement occurred, but *β-methoxyethyl isocyanate, itself, and not the substituted urea* was obtained. It appeared as an oil which was so slowly hydrolyzed by boiling water that it could be separated from the solution directly and almost quantitatively.

The synthesis of methoxyethyl isocyanate offered some difficulties; it could not be obtained by the interaction of silver cyanate and methoxyethyl chloride, because of the lack of reactivity of the latter compound. It was prepared finally by heating silver cyanate with methoxyethyl iodide, $CH_3OCH_2CH_2I$, in a sealed tube at 150° for five hours, and was found to be identical with the isocyanate produced by rearrangement of the salts of acyl esters of β-methoxy-propionhydroxamic acid.

The synthesis of this isocyanate led to a study of methoxyethyl chloride and iodide and to the development of new methods for their preparation. We prepared methoxyethyl chloride satisfactorily by alkylating ethylene chlorohydrin with dimethyl sulfate.

$$HOCH_2CH_2Cl + (CH_3)_2SO_4 \longrightarrow CH_3OCH_2CH_2Cl + CH_3HSO_4 \qquad (11)$$

The failure to obtain the isocyanate from the chloride led us to turn our attention to methoxyethyl iodide as a possible reagent. It was thought that this compound might be obtained by alkylating ethylene iodohydrin with dimethyl sulfate, but the former substance was found to decompose below 70° when treated with the dimethyl sulfate. Finally, satisfactory yields of methoxyethyl iodide were secured by treating methoxyethyl chloride with sodium iodide suspended in boiling acetone.

$$CH_3OCH_2CH_2Cl + NaI \longrightarrow CH_3OCH_2CH_2I + NaCl \qquad (12)$$

Experimental Part

Preparation of Hydroxy-acethydroxamic Acid[17] (HO)$CH_2CONHOH$

Hydroxylamine was prepared by the method recently developed by Lecher and Hofmann.[18] Slightly more than the calculated amount of it dissolved in ethyl alcohol was added to 20 g. of ethyl glycollate and the solution was allowed to stand for an hour. When the alcohol was evaporated in a stream of dry air, colorless crystals of glycolhydroxamic acid remained; yield, 19 g. The acid appeared to be very difficultly soluble

[16] Knorr, *Ber.*, **37**, 3506 (1904).

[17] The copper salt of hydroxy-acethydroxamic acid was prepared by Verlardi in 1904 by treating bromo-acetaldehyde with Piloty's acid, $C_6H_5SO_2NHOH$; but he did not isolate [Verlardi, *Gazz. chim. ital.*, **34**, II, 66 (1904)] the hydroxamic acid, itself, or any other derivatives.

[18] Lecher and Hofmann, *Ber.*, **55B**, 912 (1922).

in cold alcohol; but a solution of it in boiling alcohol deposited no crystals as it cooled, even when ether was added. It was necessary to inoculate the solution and stir it vigorously to induce crystallization, and even then the precipitate formed very slowly and was flocculent. Minute needles of the acid were formed when an alcoholic solution was evaporated slowly; m. p., 85°. It is very soluble in water and insoluble in ether, in ethyl acetate, in benzene, and in ligroin.

Anal. Subs., 0.1714: N, 22.1 cc. (20°, 768 mm.); 40% KOH used. Calc.: N, 15.37. Found: 15.09.

Benzoyl Ester of Hydroxy-acethydroxamic Acid, $HOCH_2CON(H)O—COC_6H_5$.—Three g. of hydroxy-acethydroxamic acid was dissolved in the calculated amount of 3 *N* sodium hydroxide solution and 4.6 g. of benzoyl chloride was added in five portions. The mixture was constantly agitated and cooled. Six g. of the benzoyl ester was collected on a filter and washed with boiling ligroin to remove any benzoyl chloride or benzoic acid. Recrystallized from ethyl acetate and ligroin, it melted at 160.4°. It is soluble in alcohol, in acetone, and in benzene, but insoluble in water, and in ether.

Anal. Subs., 0.1847: N, 11.6 cc. (22°, 755 mm.); 40% KOH used. Calc.: N, 7.18. Found: 7.04.

Potassium Salt, $HOCH_2CON(K)—O—COC_6H_5$.—This salt was prepared by treating the benzoyl ester dissolved in alcohol with the calculated amount of potassium alcoholate. Complete precipitation of the white crystalline salt was effected by the addition of ether. A sample of the dry salt puffed when a tube containing it was plunged into an oil-bath at 125°.

Silver Salt.—The potassium salt dissolved in cold water and treated with a solution of silver nitrate gave a white silver salt.

Anal. Subs., 0.1624: Ag, 0.0579. Calc. for $C_9H_8O_4N$: Ag, 35.76. Found: 35.61.

Rearrangement of the Potassium Salt.—When a water solution containing 1.5 g. of the salt was boiled, a white precipitate formed; it weighed 1.2 g. and consisted entirely of the benzoyl ester of hydroxy-acethydroxamic acid, produced by hydrolysis of the salt, not by rearrangement.

$$HOCH_2CON(K)OCOC_6H_5 + HOH \rightleftharpoons HOCH_2CON(H)OCOC_6H_5 + KOH \quad (13)$$

None of the products of rearrangement could be detected.

When the salt was dissolved in boiling ethyl alcohol no rearrangement occurred; it was recovered unchanged. When it was heated in boiling *iso*-amyl alcohol, rearrangement occurred. The solution was evaporated and the residue extracted with ether. Evaporation of the ether extraction yielded a white crystalline solid, melting at 159–160° which proved to be *iso*-amyl allophanate, $NH_2CONHCOOC_5H_{11}$. This substance was decomposed by dilute acid to give, ammonia, carbon dioxide, and *iso*-amyl alcohol. The residue insoluble in ether was dissolved in water. One half of this solution, treated with *p*-nitro-phenylhydrazine, gave formaldehyde-*p*-nitrophenyl hydrazone, melting at 181°, and the other half, when acidified, gave benzoic acid; m. p., 121°. These tests prove that allophanic ester, formaldehyde, and potassium benzoate are the rearrangement products.

Two g. of the potassium salt was dissolved in ethyl alcohol and the solution heated at 120° in a sealed tube for four hours. The alcohol was evaporated and the residue extracted repeatedly with ether. Evaporation of the ether extraction gave ethyl allophanate; m. p., 191°.

Acetyl Ester of Hydroxy-acethydroxamic Acid, $HOCH_2CON(H)OCOCH_3$.—A sample of hydroxy-acethydroxamic acid was warmed with a slight excess of acetic an-

hydride until no red coloration was obtained with ferric chloride. When the mixture was placed over soda lime in a vacuum desiccator, it solidified. Recrystallized from hot benzene the solid gave long needles melting at 64.5°. It is soluble in acetone, in alcohol, in chloroform, in ethyl acetate, and in water. It is insoluble in ether and in ligroin.

Anal. Subs., 0.1832: N, 17.6 cc. (25°, 761 mm.; 50% KOH used). Calc.: N, 10.52. Found: 10.78.

Potassium Salt, $HOCH_2CON(K)OCOH_3$.—The acetyl ester was dissolved in methanol and treated with a slight excess of potassium methylate. Precipitation was completed by the addition of ether.

Anal. Subs., 0.1126: K_2SO_4, 0.0564. Calc. for $C_4H_6O_4NK$: K, 22.90. Found: 22.72.

The potassium salt dissolved in water and treated with a solution of silver nitrate gave a white silver salt.

Anal. Subs., 0.1038: Ag, 0.0466. Calc. for $C_4H_6O_4NAg$: Ag, 44.98. Found: 44.91.

Preparation of Methoxy-acethydroxamic Acid[19]

$CH_3OCH_2CONHOH$

Methylmethoxyacetate was obtained according to the method given by Palomaa.[20] The hydroxamic acid was prepared from the ester by the action of hydroxylamine. For details of preparation see hydroxy-acethydroxamic acid, p. 2523. Recrystallized from ethyl acetate and ligroin, it melted at 85.5°. It is soluble in acetone, in chloroform, and in water, but slightly soluble in ether.

Anal. Subs., 0.1995: N, 24.2 cc. (25°, 756 mm.); 50% KOH used. Calc.: N, 13.59. Found: 13.62.

Benzoyl Ester of Methoxy-acethydroxamic Acid, $CH_3OCH_2CON(H)OCOC_6H_5$.—This ester was prepared from methoxy-acethydroxamic acid according to the method described on p. 9. The ester was collected on a filter and washed thoroughly with boiling ligroin. Recrystallized from warm ethyl acetate it melted at 84.5°. It is soluble in the usual organic solvents but insoluble in water and in ether.

Anal. Subs., 0.2131: N, 12.3 cc. (24°, 755 mm.); 40% KOH used. Calc.: N, 6.65. Found: 6.44.

Potassium Salt, $CH_3OCH_2CON(K)OCOC_6H_5$.—Prepared from the benzoyl ester by the method previously described on p. 2524.

Anal. Subs., 0.2614: K_2SO_4, 0.0907. Calc. for $C_{10}H_{10}O_4NK$: K, 15.82. Found: 15.61.

The silver salt was prepared from the potassium salt in the usual fashion. When heated it gradually blackened and puffed a little above 100°.

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[19] Previous work on alkoxy hydroxamic acids has been limited to the preparation of anishydroxamic acid, $CH_3OC_6H_4CONHOH$, and a few of its derivatives. Lossen prepared trihydroxamic acids with anisyl and benzoyl groups. He obtained the isocyanate, $CH_3OC_6H_4NCO$, as a rearrangement product. Angeli and Angelico, and Rimini, also prepared anishydroxamic acid some years later, but they made no further study of it.

[Lossen, *Ann.*, **175,** 323 (1875). Angeli and Angelico, *Atti. accad. Lincei,* [5] **10,** 164 (1901); *Gazz. chim. ital.,* [2] **33,** 241 (1903). Rimini, *Atti. accad. Lincei,* [5] **10,** 355 (1901).]

[20] Palomaa, *Ber.*, **42,** 1300 (1900).

Anal. Subs., 0.0690: Ag, 0.0235. Calc. for $C_{10}H_{10}O_4NAg$: Ag, 34.14. Found: 34.05.

Rearrangement of the Potassium Salt.—When a tube containing a sample of the dry salt was immersed in a bath of boiling water, rearrangement occurred and drops of methoxymethyl isocyanate formed on the walls of the tube. At 120°, the salt puffed suddenly and a cloud of isocyanate was given off. This isocyanate reacted with water to give carbon dioxide, ammonia, methyl alcohol and formaldehyde. (See Equation 10, p. 7.)

Carbon dioxide was determined by heating a solution of 1.25 g. of the potassium salt in 15 cc. of water. Ten cc. of the liquid was distilled and collected in a cooled receiver, while air, free from carbon dioxide, was passed through the solution, drying train and Liebig's potash bulbs, in which carbon dioxide was absorbed.

Anal. Subs., 1.2506: CO_2, 0.2179. Calc. for $C_{10}H_{10}O_4NK$: CO_2, 17.82. Found: 17.41.

The liquid which remained in the distilling flask, when acidified with acetic acid, yielded 0.4 g. of benzoic acid. The distillate had a strong odor of methyl benzoate. The presence of formaldehyde was confirmed; the distillate gave a heavy, yellow precipitate of formaldehyde-*p*-nitrophenylhydrazone, m. p., 181°, when an acetic acid solution of *p*-nitrophenylhydrazine was added.

Acetyl Ester of Methoxy-acethydroxamic Acid, $CH_3OCH_2CON(H)OCOCH_3$.—This ester was prepared from methoxy-acethydroxamic acid by the action of acetic anhydride as described on p. 9. Recrystallized from warm benzene, it melted at 82°. It is soluble in the usual organic solvents, and insoluble in ether and in ligroin.

Anal. Subs., 0.1970: 17.2 cc. (25°, 753 mm.; 50% KOH used). Calc.: N, 9.53. Found: 9.68.

Potassium Salt, $CH_3OCH_2CON(K)OCOCH_3$.—This salt was prepared from the acetyl ester by the addition of potassium methylate. When a small sample in a tube was heated in a bath of boiling water, it puffed and methoxymethyl isocyanate collected on the walls of the tube, leaving potassium benzoate as a residue.

Anal. Subs., 0.1638: K_2SO_4, 0.1029. Calc. for $C_5H_8O_4NK$: K, 21.08. Found: 21.19.

An ice-cold solution from the potassium salt treated with silver nitrate gave a white silver salt.

Anal. Subs., 0.0917: Ag, 0.0479. Calc. for $C_5H_8O_4NAg$: Ag, 42.52. Found: 42.34.

Methoxymethyl Isocyanate, CH_3OCH_2NCO.—This isocyanate, obtained as a rearrangement product of the potassium salt (p. 7), is a new compound. It was prepared as follows. Silver cyanate was made from urea and silver nitrate according to the method described by Dean.[21] The product was dried in a vacuum over sulfuric acid. A solution of 25 g. of freshly distilled chloromethyl ether in 100 cc. of absolute ether was placed in a flask attached to a reflux condenser; then 44 g. of dry, very finely powdered silver cyanate was introduced slowly in 5g. portions. Considerable heat was evolved, so the flask was cooled in an ice-salt mixture. All the salt should be added within half an hour. The mixture was shaken for the next half-hour.

At the end of this time, the ether solution was filtered directly into a distilling flask and the silver chloride was washed twice with ether. The ether was distilled and the isocyanate collected at 87°. A small amount was left in the distilling flask probably as the polymer. The corrected boiling point was found to be 87.5°.

[21] Dean, *J. Chem. Soc.*, **85**, 1371 (1904).

Methoxymethyl isocyanate is a heavy, colorless oil. It is a powerful lachrymator. It reacts with water to give carbon dioxide, ammonia, methyl alcohol and formaldehyde. When it is allowed to stand for a few days it polymerizes to give a white, vitreous solid. It reacts to form substituted ureas when treated with an ether solution of dimethylamine, of aniline, or of methyl aniline. It gives a semicarbazide when added to a cold ether solution of phenylhydrazine. These products are crystalline substances. We expect to study them in more detail later.

Anal. Subs., 0.1277: 18.5 cc. (25°, 758 mm.; 40% KOH used). Calc. for $C_3H_5O_2N$: N, 16.09. Found: 16.40.

Decomposition of Methoxymethyl Isocyanate by Water.—A sample of methoxymethyl isocyanate weighing 1.261 g. was added to 11 cc. of water containing 3 cc. of dil. acetic acid, and the solution was warmed until evolution of carbon dioxide ceased. When the product was poured into a cold acetic acid solution of *p*-nitro-phenylhydrazine, 2.179 g. of formaldehyde-*p*-nitro-phenylhydrazone was obtained, or 92% of the amount calculated from the equation,

$$\left.\begin{array}{l} CH_3OCH_2NCO + H_2O = CH_3OCH_2NH_2 + CO_2 \\ CH_3OCH_2NH_2 + H_2O = HCHO + CH_3OH + NH_3 \end{array}\right\} (14)$$

Anal. Subs., 1.2610: $NO_2C_6H_4NHN{=}CH_2$, 2.179. Calc. for $C_3H_5O_2N$: CH_2O, 34.46. Found: 31.86.

Another sample of methoxymethyl isocyanate was decomposed by water in a stream of air free from carbon dioxide. The carbon dioxide evolved was passed through a drying train and adsorbed in Liebig's potash bulbs.

Anal. Subs., 0.7675: CO_2, 0.3859. Calc. for $C_3H_5O_2N$: CO_2, 50.61. Found: 50.34.

There was no evidence of the formation of symmetrical methoxymethyl urea under these conditions.

Attempts to Prepare Methoxymethylamine.—Methoxymethyl-phthalimide was prepared according to Hopkins' method[22] from bromomethyl-phthalimide and methyl alcohol. The methoxymethyl-phthalimide was hydrolyzed under conditions as mild as possible, but only the decomposition products, ammonia, methanol and formaldehyde could be isolated.

Chloromethyl-methyl ether was slowly added to a cold solution of ammonia in ether. The white crystalline precipitate which separated was collected on a filter in the absence of moisture and dried in a vacuum. This product was chiefly ammonium chloride; a small amount of substance having the properties of hexamethylene-tetramine was also obtained. No trace of any methoxymethylammonium chloride, $(CH_3OCH_2)NH_3Cl$, could be detected.

Ethoxy-acethydroxamic Acid

$C_2H_5OCH_2CONHOH$

Ethyl ethoxyacetate was obtained from ethyl chloro-acetate and sodium ethylate according to the method described by Schreiner.[23] Ethoxy-acethydroxamic acid was prepared by the action of hydroxylamine on ethyl ethoxyacetate according to the method described above (p. 8). Since the solid obtained by evaporation of the alcohol was a viscous material which could not be purified by recrystallizing it from solvents, it was converted into the copper salt by treating a solution of it in water with a saturated solution of copper acetate. The copper salt, collected on a filter and dried in a vacuum over sulfuric acid, was powdered and suspended in methanol. A stream of dry hydrogen

[22] Hopkins, *J. Am. Chem. Soc.*, **45**, 541 (1923).

[23] Schreiner, *Ann.*, **197**, 1 (1879).

sulfide was passed through the liquid until the precipitation of the copper sulfide was complete. The solution was filtered and evaporated in a stream of dry air. Several crystallizations of the acid gave a product melting between 74° and 76°. In the course of a few days the acid softened appreciably. It is soluble in acetone and in water and slightly soluble in ether, in warm benzene and in warm ethyl acetate.

Anal. Subs., 0.1187: N, 12.7 cc. (23°, 762 mm.; 40% KOH used). Calc.: N, 11.77. Found: 12.08.

Ethoxy-acethydroxamic acid was also prepared by treating ethoxyacetyl chloride with hydroxylamine. Ethoxyacetyl chloride was made by the action of thionyl chloride upon ethoxyacetic acid.[24] This acid chloride was dissolved in benzene, and a slight excess of solid hydroxylamine was added. When the mixture had stood for three hours, the reaction was complete; so the solution was heated to boiling and filtered. The hydroxamic acid crystallized from the cold filtrate. An additional amount was obtained by extracting the precipitate with hot benzene.

Benzoyl Ester of Ethoxy-acethydroxamic Acid, $C_2H_5OCH_2CON(H)OCOC_6H_5$.—This ester, prepared by the usual method, when recrystallized from alcohol and water, melted sharply at 156°. It is soluble in acetone, in benzene, and ethyl acetate; and insoluble in ligroin and in water.

Anal. Subs., 0.1723: N, 9.4 cc. (23°, 752 mm.; 40% KOH used). Calc.: N, 6.26. Found: 6.11.

Potassium Salt, $C_2H_5OCH_2CON(K)OCOC_6H_5$.—Prepared from the benzoyl ester according to the method described above. In a small tube, a freshly prepared sample of the salt puffed at 115°.

Anal. Subs., 0.2808: K_2SO_4, 0.0921. Calc. for $C_{11}H_{12}O_4NK$: K, 14.95. Found: 14.69.

Rearrangement of the Potassium Salt.—When 1.7691 g. of the potassium salt was dissolved in boiling water, it suffered rearrangement to give carbon dioxide, ammonia, ethyl alcohol, formaldehyde and potassium benzoate. Carbon dioxide was determined by adsorption in Liebig's potash bulbs as described on p. 11.

Anal. Subs., 1.7691: CO_2, 0.2903. Calc. for $C_{11}H_{12}O_4NK$: CO_2, 16.86. Found: 16.41.

$$C_2H_5OCH_2CON(K)OCOC_6H_5 + 2H_2O \longrightarrow C_2H_5OH + H_2C{=}O + CO_2 + NH_3 + C_6H_5COOK \quad (15)$$

One half the solution containing the other rearrangement products, when acidified, gave a precipitate of benzoic acid; m. p., 121°. The other half added to an acetic acid solution of *p*-nitro-phenylhydrazine gave yellow crystals of formaldehyde-*p*-nitro-phenylhydrazone; m. p., 181°.

In another experiment a solution containing the rearrangement products of the potassium salt was distilled, and the first fraction of the distillate was added to a little freshly prepared 3,5-dinitro-benzoyl chloride. The ester obtained melted at 92–93° which confirmed the presence of ethyl alcohol.

Acetyl Ester of Ethoxy-acethydroxamic Acid, $C_2H_5OCH_2CON(H)OCOCH_3$.—This ester was prepared by the usual method from ethoxy-acethydroxamic acid and acetic anhydride. It crystallized from benzene in long, colorless needles; m. p., 84°. It is soluble in alcohol, in acetone, in ethyl acetate and in water, and very slightly soluble in ether and in ligroin.

Anal. Subs., 0.2047: N, 15.8 cc. (24°, 760 mm.); 40% KOH used. Calc.: N, 8.70. Found: 8.78.

[24] Sommelet, *Ann. chim.*, [8] **9**, 488 (1906).

Potassium Salt, $C_2H_5OCH_2CON(K)OCOCH_3$.—No precautions were necessary in the preparation of the potassium salt.

Anal. Subs., 0.1560: K_2SO_4, 0.0698. Calc. for $C_6H_{10}O_4NK$: K, 19.60. Found: 20.03.

Ethoxymethyl Isocyanate, $C_2H_5OCH_2NCO$.—This substance was prepared from silver cyanate and chloromethyl ethyl ether according to the method described for methoxymethyl isocyanate. It distilled between 105° and 106°.

Anal. Subs., 0.1393: N, 16.4 cc. (24°, 762 mm.); 40% KOH used. Calc.: N, 13.86. Found: 13.81.

Ethoxymethyl isocyanate is a powerful lachrymator. It is a colorless liquid and is decomposed by water to give carbon dioxide, ammonia, formaldehyde and ethyl alcohol. Carbon dioxide was absorbed in Liebig's potash bulbs as described above.

Anal. Subs., 0.6814. CO_2, 0.2964. Calc. for $C_4H_7O_2N$: CO_2, 43.56. Found: 43.50.

The other products of hydrolysis were determined as follows: formaldehyde as formaldehyde-*p*-nitro-phenylhydrazone; ethyl alcohol as ethyl-3,5-dinitrobenzoate.

It reacted to form substituted ureas when it was treated with ether solutions containing the calculated amount of dimethylamine, of methyl aniline or of aniline.

Attempts to prepare ethoxymethylamine from ethoxymethyl-phthalamide and from chloromethyl ethyl ether and ammonia gave, as in the case of the methoxy derivative, only the decomposition products, ammonia, formaldehyde and ethyl alcohol.

Beta-Methoxy-propionhydroxamic Acid

$CH_3OCH_2CH_2CONHOH$

Methyl β-methoxypropionate was chosen as the starting material in the preparation of the β-methoxy-propionhydroxamic acid.

Purdie and Marshall[25] prepared this ester by treating methyl acrylate with sodium methylate. The product which they obtained was extracted with ether, the ether removed and the ester distilled between 140° and 145°. This ester was analyzed and found to contain methyl alcohol, but they make no mention of the boiling point of the ester finally purified.

Pure methyl β-methoxypropionate was secured as follows. Eleven and three-tenths g. of sodium was added to 150 cc. of methanol in a flask attached to a reflux condenser. While the solution was still warm from the reaction with the sodium, 60 g. of methyl β-chloropropionate was allowed to drop into the sodium methylate just fast enough to keep the solution boiling gently. After all the ester had run in, the mixture was refluxed for an hour and allowed to stand during the night. The alcoholic solution of the ester, carefully decanted from the salt, was saturated with carbon dioxide to decompose any unconverted sodium methylate. The salt residue was shaken with 50 cc. of ether, collected on a filter and washed with ether until it was pure white. The filtrate and washings were combined, and added to the main alcohol solution. The alcohol was removed by distillation under diminished pressure and the residue fractionated. The ester distilled between 144° and 145° (760 mm.).

Preparation of β-Methoxy-propionhydroxamic Acid.—This acid was prepared from methyl β-methoxypropionate by treating it with hydroxylamine in alcohol solution. After several hours the alcohol was removed. The resulting solid was dissolved in water and converted into the copper salt from which the hydroxamic acid was obtained by the action of hydrogen sulfide as given for the preparation of ethoxy-acethydroxamic acid.

[25] Purdie and Marshall, *J. Chem. Soc.*, **59**, 474 (1891).

β-Methoxy-propionhydroxamic acid, recrystallized from alcohol, melts at 93–95°. It is very soluble in water and slightly soluble in ethyl acetate, in ether, in chloroform and in ligroin.

Anal. Subs., 0.2916: N, 30.5 cc. (22°, 752 mm.); 40% KOH used. Calc.: N, 11.77. Found: 11.59.

To prepare β-methoxypropionyl chloride, it was necessary to obtain β-methoxypropionic acid. This acid has not been described previously. The calcium salt was isolated by Purdie and Marshall[26] from sodium β-methoxypropionate which they obtained by the action of methyl acrylate upon sodium methylate.

Preparation of β-Methoxypropionic Acid.—A solution of 50 g. of β-chloropropionic acid in 100 cc. of methanol was allowed to drop into 300 cc. of methanol, previously treated with 21.3 g. of sodium, just fast enough to keep the solution boiling gently. The mixture was refluxed for two hours and allowed to stand overnight. The alcohol was distilled and the last traces were removed under diminished pressure. The dry sodium salt of β-methoxypropionic acid that remained in the flask was powdered thoroughly and 46 cc. of concd. hydrochloric acid (d., 1.18; 37%) was added slowly while the salt was stirred and cooled in an ice mixture. Sodium chloride was collected on a filter and washed throughly with ether. The filtrate was extracted thrice with 50 cc. of ether. The extractions were combined with the ether used to wash the sodium chloride and dried over anhydrous sodium sulfate. The ether was evaporated and the acid distilled at 126° under 30 mm. pressure; yield, 60%.

Preparation of β-Methoxypropionyl Chloride, $CH_3OCH_2CH_2COCl$.—Twenty g. of β-methoxypropionic acid was treated with 22 g. of pure, colorless, thionyl chloride, in a small flask connected to a reflux condenser. The reaction proceeded slowly at room temperature and rapidly at 70°. The mixture, heated for half an hour at 70°, gave β-methoxypropionyl chloride distilling at 135–136° (758 mm.).

Two equivalents of free hydroxylamine were added to a solution of β-methoxypropionic chloride in benzene. The mixture was shaken vigorously and allowed to stand for several hours. It was then heated and filtered from the hydroxylammonium chloride. As the filtrate cooled, crystals of β-methoxypropionhydroxamic acid separated; yield, almost quantitative.

Benzoyl Ester of β-Methoxy-propionhydroxamic Acid, $CH_3OCH_2CH_2CON(H)OCOC_6H_5$.—This ester was prepared according to the usual method. Recrystallized from methanol and water it melted at 148°. It is soluble in acetone, in ethyl alcohol, in ethyl acetate and in benzene.

Anal. Subs., 0.2041: N, 11.1 cc. (21°, 755 mm.; 40% KOH used). Calc.: N, 6.26. Found: 6.14.

Potassium Salt, $CH_3OCH_2CH_2CON(K)OCOC_6H_5$.—This salt was prepared from the benzoyl ester by the usual method. A sample of the dry salt, in a small tube, puffed when it was plunged into an oil-bath at 110°.

Anal. Subs., 0.1318: K_2SO_4, 0.0434. Calc. for $C_{11}H_{12}O_4NK$: K, 14.95. Found: 14.76.

Rearrangement of the Potassium Salt.—When a solution of the potassium salt in water was boiled for a short time, an oil formed slowly. This oil, separated and dried, distilled between 120° and 125°, and corresponded in properties with β-methoxyethyl isocyanate, $CH_3OCH_2CH_2NCO$, prepared by the action of methoxyethyl iodide upon silver cyanate and described later in this article. The isocyanate was found to be practically insoluble in water. The aqueous solution from which the isocyanate separated, when acidified, gave a precipitate of benzoic acid.

[26] Ref. 25, p. 475.

Acetyl Ester of β-Methoxy-propionhydroxamic Acid, $CH_3OCH_2CH_2CONHOCOCH_3$.—This ester was prepared according to the usual method. It crystallized from warm benzene in long, colorless needles, melting sharply at 86°. It is soluble in the ordinary organic solvents and is almost insoluble in ether and in ligroin.

Anal. Subs., 0.2113: N, 16.0 cc. (22°, 760 mm.; 40% KOH used). Calc. for $C_6H_{11}O_4N$: N, 8.70. Found: 8.61.

Potassium Salt, $CH_3OCH_2CH_2CON(K)OCOCH_3$.—No precautions were necessary in the preparation of this salt. When treated with an aqueous solution of silver nitrate, it gave the silver salt.

Anal. Subs., 0.1061: K_2SO_4, 0.0466. Calc. for $C_6H_{10}O_4NK$: K, 19.60. Found: 19.23.

Beta-methoxyethyl Isocyanate, $CH_3OCH_2CH_2NCO$.—This isocyanate is a new compound. It was synthesized by treating β-methoxyethyl iodide with silver cyanate. A study of the preparation and properties of methoxyethyl chloride and methoxyethyl iodide was necessary as a preliminary to its synthesis.

Preparation of Methoxyethyl Chloride, $CH_3OCH_2CH_2Cl$.—This compound was prepared previously by Fileti and Gaspari[27] by treating chloromethyl methyl ether with zinc. They obtained a small yield of methoxyethyl chloride boiling at 92°. We have developed a new method for its preparation which gives yields of over 60%. Eighty g. of redistilled ethylene chlorohydrin and 126 g. of dimethyl sulfate (distilled at 98° and 30 mm.) were mixed in a 500cc. distilling flask, connected with a condenser attached to a receiving vessel. When the flask was heated in an oil-bath to 120°, slow distillation of the methoxyethyl chloride took place. The thermometer in the neck of the distilling flask registered 90–95°. A steady rate of distillation could be maintained by gradually raising the temperature of the oil-bath to 150°. The temperature of the bath was held at 150° until distillation had practically stopped.

At this stage the mixture was allowed to cool and a 20% solution of sodium hydroxide, one-half an equivalent calculated on the basis of the dimethyl sulfate, was carefully added. When the bath was heated a second time to 150° an additional amount of methoxyethyl chloride was obtained. The bath should not be heated above 160°; above this temperature rapid decomposition may occur. Alkali cannot be added at the beginning of this reaction since it decomposes the ethylene chlorohydrin; and when it is added towards the close of the reaction care must be taken not to allow the solution to become alkaline.

The methoxyethyl chloride was washed twice with a 20% solution of sodium hydroxide and dried over anhydrous sodium sulfate. The dry chloro ether was distilled first over solid sodium hydroxide; when redistilled it boiled sharply at 93°. It is interesting to note that chloromethylethyl ether, $C_2H_5OCH_2Cl$, an isomeric compound, decomposes somewhat on distillation, is very reactive, is decomposed by water and cannot be kept for any length of time; while this isomer, methoxyethyl chloride, distils without decomposition, does not react with sodium or zinc even at 140° and is not affected appreciably by boiling water.

We found that methoxyethyl chloride did not react with silver cyanate to give an isocyanate even at 150°. No reaction could be effected with silver cyanate under experimental conditions which would not decompose the chloro ether or the isocyanate. Even when silver cyanate and methoxyethyl chloride were heated in a sealed tube at 140° for four hours, the recovery of the chloride was practically quantitative.

Preparation of Methoxyethyl Iodide, $CH_3OCH_2CH_2I$.—It was thought that this compound might be prepared by alkylating ethylene iodohydrin with dimethyl sulfate,

[27] Fileti and Gaspari, *Gazz. chim. ital.*, **27**, II, 293 (1897).

just as we prepared methoxyethyl chloride. Ethylene iodohydrin was made according to the method of Wieland and Sakellarios[28] by treating ethylene chlorohydrin with sodium iodide suspended in boiling acetone. When this product was treated with dimethyl sulfate, even at room temperature decomposition occurred. No methoxyethyl iodide could be secured in this way.

Karvonen[29] had prepared methoxyethyl iodide by heating ethylene iodide with methyl alcohol in a sealed tube at 100°. A very small yield of methoxyethyl iodide distilled without decomposition at 137°. This method of preparation necessitated the rather long preparation of ethylene iodide and gave only very small amounts. We have found a new method of preparation which gives very satisfactory yields.

Fifty g. of redistilled methoxyethyl chloride was added to 90 g. of anhydrous sodium iodide suspended in 120 g. of acetone. This mixture was refluxed for 15 hours, cooled, and the salt separated. The acetone was evaporated under diminished pressure until precipitation of the sodium halides occurred. These salts were separated and the filtrate was treated with an equal volume of water. The lower layer of methoxyethyl iodide was separated, washed several times with water, dried over anhydrous sodium sulfate, and distilled over solid sodium hydroxide. Methoxyethyl iodide distils between 137° and 138°, and is a heavy colorless liquid, with a pleasant odor. It reacts with silver nitrate very slowly and does not react with sodium at ordinary temperature. Yield, 80%.

Methoxyethyl Isocyanate, $CH_3OCH_2CH_2NCO$.—No reaction occurred when methoxyethyl iodide and a suspension of silver cyanate in ether were heated in a sealed tube at 110°. The iodide was recovered quantitatively. The reaction proceeded slowly at 130°. When the mixture was heated at 150° for five hours, the conversion into isocyanate was practically complete.

Twenty-five g. of methoxyethyl iodide was added to 20 g. of pure dry silver cyanate in a glass tube; 50 cc. of ether was added to this mixture, the tube was sealed and heated in an electric furnace for five hours at 148°. The tube was cooled and opened and its contents were filtered directly into a distilling flask. The silver iodide on the filter was washed with ether. After the ether was distilled, the thermometer rose sharply to 122°, and the isocyanate distilled between 123° and 124°; yield, 80%.

Methoxyethyl isocyanate is a colorless oil which reacts very slowly with water at ordinary temperature. It has a sharp, penetrating odor and is a strong lachrymator.

Anal. Subs., 0.1217: N, 14.8 cc. (22°, 753 mm.); 40% KOH. Calc. for $C_4H_7O_2N$: N, 13.86. Found: 13.72.

Summary

The preparation and properties of the following new hydroxamic acids, together with their benzoyl and acetyl esters, are described: hydroxy-acethydroxamic acid; methoxy-acethydroxamic acid; ethoxy-acethydroxamic acid; β-methoxy-propionhydroxamic acid. The potassium and silver salts of many of the acyl esters were made, and conditions under which they rearranged were determined.

The following hypothesis has been advanced. Any substance (hydroxamic acid, acid azide or bromo-amide) which has an hydroxyl group in the α position, when it undergoes rearrangement of the Lossen-Curtius-Hofmann type will give an aldehyde or ketone and cyanic acid. If the rearrangement takes place in aqueous solution, cyanic acid will yield urea

[28] Wieland and Sakellarios, *Ber.*, **53**, 208 (1920).

[29] Karvonen, *Ber.*, **42**, 690 (1909).

or ammonia and carbon dioxide; if it takes place in alcohol solution an allophanic ester will be produced.

The dry salts of the acyl esters of the alkoxyhydroxamic acids described above, when heated, rearranged to give new isocyanates: methoxymethyl isocyanate; ethoxymethyl isocyanate; β-methoxyethyl isocyanate. The rearrangement of these salts in water solution did not yield *sym*-disubstituted ureas, since methoxymethyl isocyanate and ethoxymethyl isocyanate, upon hydrolysis, yield amines, $ROCH_2NH_2$, which dissociate at once to give ammonia, formaldehyde and an alcohol, while β-methoxyethyl isocyanate was unaffected by water and was isolated as such when the compound, $CH_3OCH_2CH_2—CON(K)OCOC_6H_5$, was heated with water.

During the investigation new methods for the preparation of methoxyethyl chloride and methoxyethyl iodide were developed, and the following additional new compounds were synthesized: methoxymethyl isocyanate, ethoxymethyl isocyanate, β-methoxyethyl isocyanate, β-methoxypropionic acid and β-methoxypropionyl chloride.

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